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EXAMINER	
SCHNIZER, RICHARD A	

ART UNIT	PAPER NUMBER
1635	

DATE MAILED: 01/30/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/875,228	YU ET AL.	
	Examin r	Art Unit	
	Richard Schnizer, Ph. D	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 November 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-14,31,32,54,69,71,73 and 75* is/are pending in the application.

4a) Of the above claim(s) *54,69,71,73 and 75* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *1-14,31 and 32* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *22 October 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *12/27/01* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

An amendment was received and entered on 11/6/03. Applicant's election with traverse of group 1, claims 1-14 is acknowledged. Applicant traverses the restriction of claims 31 and 32, drawn to adenoviral vectors comprising an adenoviral gene under control of a hKLK2-TRE, from claims 1-14, drawn to hKLK-TREs. After further consideration, claims 31 and 32 are rejoined.

Claims 1-14, 31, 32, 54, 69, 71, 73, and 75 are pending.

Claims 54, 69, 71, 73, and 75 are withdrawn because they are drawn to nonelected subject matter. Applicant did not traverse the restriction of claims 54, 69, 71, 73, and 75, and the restriction is made FINAL.

Claims 1-14, 31, and 32 are under consideration in this Office Action.

Drawings

Applicant has submitted drawings which are adequate for the purpose of examination, but which may not be deemed acceptable for publication after review by a draftsperson.

Claim Objections

Claims 2-5 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. These claims are drawn to polynucleotides comprising 150 contiguous nucleotides of a reference sequence, and require that "said 150 contiguous nucleotides comprises

nucleotides found within" various fragments of SEQ ID NO:1. However, because the polynucleotides in question are all composed of the same 4 nucleotides, and each of the recited fragments of SEQ ID NO:1 comprises all 4 nucleotides, the limitation "said 150 contiguous nucleotides comprises nucleotides found within [a fragment of SEQ ID NO: 1]" does not further limit claim 1. It is suggested that the words "comprises nucleotides" in claims 2-5 should be deleted and replaced by the word "are".

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-14, 32, and 33 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-21 and 24-31 of US Patent 6,676,935, or claims 1-17 of US Patent No. 6,432,700, or claims 1-8 and 11-15 of US Patent 6,495,130. Although the conflicting claims are not identical, they are not patentably distinct from each other.

US Patent 6,676,935 claims adenoviral vectors comprising an adenoviral gene required for adenoviral replication, wherein the gene is operably linked to a TRE. The specification teaches that a TRE may be an hKLK2-TRE, such as that in SEQ ID NO:3 of '935. See paragraphs 13, and 77, and Fig. 14. It would have been obvious to one of ordinary skill in the art at the time of the invention to use the hKLK2-TRE of '935 because the claims of '935 suggest the use of a TRE, and the specification exemplifies the hKLK2-TRE. Thus the invention as a whole was prima facie obvious.

US Patent 6,432,700 claims adenoviral vectors comprising an adenoviral gene required for adenoviral replication, wherein the gene is operably linked to a TRE. The specification teaches that a TRE may be an hKLK2-TRE, such as that in SEQ ID NO:3 of '700. See paragraphs 4,5, and 80. It would have been obvious to one of ordinary skill in the art at the time of the invention to use the hKLK2-TRE of '700because the claims of '700 suggest the use of a TRE, and the specification exemplifies the hKLK2-TRE. Thus the invention as a whole was prima facie obvious.

US Patent 6,495,130 claims adenoviral vectors comprising an adenoviral gene required for adenoviral replication, wherein the gene is operably linked to a TRE. The specification teaches that a TRE may be an hKLK2-TRE, such as that in SEQ ID NO:11 of '130. See paragraphs 22, 83, 93 and 95. SEQ ID NO:11 of '130 is identical to instant SEQ ID NO:1. It would have been obvious to one of ordinary skill in the art to use the hKLK2-TRE of '130 because the claims of '130 suggest the use of a TRE, and the specification exemplifies the hKLK2-TRE. Thus the invention as a whole was prima facie obvious.

Claims 14, 31 and 32 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-20 and 22-26 of US Patent 6,436,394, or claims 1-26 and 28-54 of US Patent 6,197,293.

US Patent 6,436,394 claims adenoviral vectors comprising an hKLK2-TRE operably linked to an adenoviral gene required for replication, see e.g. claim 13.

US Patent 6,197,293 claims adenoviral vectors comprising an adenoviral gene required for replication under control of a TRE. The specification teaches that the TRE may be an hKLK2-TRE. See paragraph 16.

While the issued claims are not coextensive in scope with the instant claims, they do represent species of the instant claims, thereby rendering it obvious.

Claims 14 is rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-11 of US Patent 6,051,417.

US Patent 6,051,417 claims expression constructs comprising a promoter and an hKLK2-TRE.

While the issued claims are not coextensive in scope with the instant claim, they represent species of the instant claim, thereby rendering it obvious.

Claims 1-13 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-22 of U.S. Patent No. 6,585,968, or claims 1-20 and 22-26 of US Patent 6,436,394, or claims 1-26 and 28-54

of US Patent 6,197,293, in view of any one of US Patents 6,676,935, or 6,432,700, or 6,495,130.

US Patent 6,585,968 claims adenoviral vectors comprising an hKLK2-TRE operably linked to an adenoviral gene required for replication, see e.g. claim 22.

US Patent 6,436,394 claims adenoviral vectors comprising an hKLK2-TRE operably linked to an adenoviral gene required for replication, see e.g. claim 13.

US Patent 6,197,293 claims adenoviral vectors comprising adenoviral genes required for replication, wherein the genes are under control of TREs. The specification teaches that the TRE may be an hKLK2-TRE. See paragraph 16.

None of these patents teaches instant SEQ ID NO:1.

U.S. Patents 6,676,935, 6,432,700, and 6,495,130, teach SEQ ID NOS: 3, 3, and 11, respectively, each of which is identical to instant SEQ ID NO:1. It would have been obvious to one of ordinary skill in the art to use in the inventions of the '968, '394, or '293 patents the hKLK2-TRE disclosed in U.S. Patents 6,676,935, or 6,432,700, or 6,495,130, because one could reasonably expect this hKLK2-TRE to function in an adenoviral vector in view of the teachings of these patents, each of which suggests the use of this sequence in an adenoviral vector, operably linked to a gene required for viral replication.

Claims 1-13 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-11 of U.S. Patent No. 6,051,417, in view of any one of US Patents 6,676,935, or 6,432,700, or 6,495,130.

US Patent 6,051,417 claims methods of screening for compounds which alter expression of a prostate-specific enhancer from a human glandular kallikrein (hKLK2) gene, said method employing cells containing an expression construct, said expression construct comprising a transcriptional initiation region of a prostate specific enhancer from a human glandular kallikrein (hKLK2) gene and a promoter and a marker gene whose expression product provides a detectable signal, wherein said marker gene is under the transcriptional control of said transcriptional initiation region

US Patent 6,051,417 does not teach instant SEQ ID NO:1.

US Patents 6,676,935, 6,432,700, and 6,495,130, teach SEQ ID NOS: 3, 3, and 11, respectively, each of which is identical to instant SEQ ID NO:1. It would have been obvious to one of ordinary skill in the art to use the hKLK2-TRE disclosed in U.S. Patents 6,676,935, or 6,432,700, or 6,495,130, because one could reasonably expect this hKLK2-TRE to function in the method of 6,051,417 in view of the teachings of these patents.

Claims 1-14, 31, and 32 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-28 of copending published US Application 20030152553 , or claims 1-9, 19, 22, 26-39, 41, 49-55, 59-63, 67, and 68 of copending published US Application 20030118555, or claims 1-12, 14, 18-28, 41-43, and 47-58 of copending published US Application 20030068307. Although the conflicting claims are not identical, they are not patentably distinct from each other.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Each of the cited Applications claims adenoviral vectors comprising an hKLK2-TRE o9erably linked to a gene required for viral replication. Each of the Applications discloses instant SEQ ID NO:1 as an example of an hKLK2-TRE, therefore it would have been obvious to use instant SEQ ID NO: 1 as an hKLK2-TRE in the inventions of each of these Applications.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 7 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 7 is indefinite because it is unclear what are the metes and bounds of "stringent conditions". The specification gives a non-limiting definition at paragraphs 112 and 117, but the definition of "stringent" hybridization conditions varies from laboratory to laboratory, and the term has no single art-recognized definition, so one cannot know the metes and bounds of the claims. Additionally the specification teaches the use of 6M SSC in stringent hybridization conditions at paragraph 112. However, SSC is not a single compound but a solution of several different compounds, generally made up as a 20X stock solution, so it is inappropriate to refer to an SSC solution in terms of molarity

without stipulating to what molecular component one refers. As such one of skill in the art cannot know to what concentration of SSC the specification refers in paragraph 112, and cannot know what is intended by stringent conditions". Finally, one of skill in the art appreciates that a critical determinant of the results of hybridization procedures is the conditions under which the membrane is washed. However, the claim recites no washing conditions, so one of skill in the art could not know what is the scope of sequences that would remain bound to the target after completion of the hybridization protocol.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Written Description

Claim 1-7, 31, and 32 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 1-5 are drawn to isolated polynucleotides with enhancer function. The nucleic acids must have 150 contiguous nucleic acids from SEQ ID NO:1 that are not present in SEQ ID NOS: 2 or 3, but there is no requirement that the enhancer function must reside in these 150 contiguous nucleotides, and no structural limitation on the portion of the claimed nucleic acid that must have enhancer activity. The claims do not

limit the identity of the cell type in which the enhancer is active, or the transcription factor binding sites it must contain. As a result, these clams embrace any enhancer sequence, known or unknown, that is active in any tissue or cell type, with the sole structural requirement that the enhancer must be linked to, or found within, 150 contiguous nucleotides of SEQ ID NO:1. Claim 6 is similar to claims 1-5, except that the structural limitation is broader, i.e. the isolated polynucleotides must comprise 150 contiguous nucleotides that are 70% identical to a sequence from SEQ ID NO:1. Claims 8-13 are similar to claims 1-5 except that the structural limitation is somewhat narrower because the claimed polynucleotides must comprise specific fragments of SEQ ID NO:1. These claims are not included in the rejection because the fragments of SEQ ID NO:1 recited in claims 8-13 contain an enhancer, whereas the fragments of SEQ ID NO:1 recited in claims 1-6 need not comprise an enhancer. Note that none of claims 1-6 requires any correlation between structure and activity. That is, none of these claims requires that the enhancer activity must reside within the portion of the claimed polynucleotide that is limited to a particular sequence. Further, none of the claims limits the types of tissues or cells in which the enhancer is active, or the transcription factor binding sites it must contain.

A review of the specification shows that Applicant considers the invention to be a prostate-specific enhancer located within SEQ ID NO:1 that is active in prostate cells bearing androgen receptors. SEQ ID NO:1 contains an enhancer which is active in prostate cells expressing androgen receptors (LNCaP), but inactive in prostate cells lacking androgen receptors (PC-3). Ectopic expression of androgen receptors in PC-3

cells was not sufficient to provide androgen-sensitive enhancer activity in PC-3 cells, indicating that LNCaP cells have some other characteristic that is required for activity of the SEQ ID NO:1 enhancer. See paragraph 367.

The specification discloses a single species of the claimed invention, and several active fragments of that species. Deletion analysis of SEQ ID NO:1 defines a core enhancer of 1172 bases from position 7200-8371 that has full enhancer activity (about 90-fold induction in LNCaP cells when linked to a minimal promoter). A minimal fragment from position 8021-8371 has reduced activity, (37-fold induction). A fragment from position 8128-8263 did not show any enhancer activity. See pages 101 and 102, and Figs. 24A and 24B. The specification discloses an androgen response element at position 8192-8206 of SEQ ID NO:1 that is necessary but not sufficient for enhancer function. Two different mutated versions of this ARE eliminate enhancer activity when located in normal context within nucleotides 7200-8371 (the maximally active core enhancer fragment of SEQ ID NO:1). This ARE is located within the inactive 8128-8263 fragment, so it is not sufficient for activity. See page 103, line 4 to page 104, line 6, and Fig. 11.

The prior art teaches a wide variety of enhancers that are active in a wide variety of specific tissues. For example, liver-, kidney-, neuron-, and T cell-specific enhancers were well known prior to the time of the invention. (See e.g., Trujillo et al (PNAS 88: 3797-3801, 1991), Igrahachi et al (J. Biol. Chem. 271(16): 9666-9674, 1996), Charron et al (J. Biol. Chem. 270(51): 30604-30610, 1995), and Wotton et al (J. Biol. Chem. 270(13): 7515-7522, 1995)). These enhancers comprise different sequences that bind

different transcription factors that are expressed in a tissue specific manner. Thus the claimed genus of enhancers in general is very broad. The specification fails to define any structural features that are common to the broad genus of enhancers that are active in various cell and tissue types.

The specification does not provide an adequate description for the claimed genus because the genus is not defined by its structure, or by any correlation between structure and function, instead the claimed genus is defined by its function only, i.e. enhancer activity. The claims make no requirement that the portion of the claimed polynucleotide that comprises enhancer activity must have any particular structural characteristics. The only functional characteristic required is that the polynucleotide must have enhancer activity. The courts have found that in the case of claims to nucleic acids encoding genes, a definition of gene function does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is. See *Regents of the Univ. Calif. v. Eli Lilly & Co.*, 43 USPQ2d 1398 (CA FC, 1997)). It follows that a generic statement such as "a polynucleotide having enhancer activity" is not an adequate written description of a genus because it does not distinguish the genus from others. The fact that the enhancer must be linked to a defined sequence does not limit the genus of enhancers that is embraced because any enhancer sequence can be artificially linked to any other sequence. The rejection of claims 1-6 could be overcome by linking a required function with a required structure, i.e. wherein the required structure has enhancer activity.

Claim 7 is drawn to the genus of isolated polynucleotides having at least about 15 nucleotides that hybridize under stringent conditions to a polynucleotide comprising nucleotides 1-11407 of SEQ ID NO:1, wherein the at least about 15 nucleotides are not depicted in SEQ ID NOS: 2 or 3. In other words, claim 7 embraces any 15mer or greater, not present in SEQ ID NOS: 2 or 3, that hybridizes under stringent conditions to any polynucleotide that is linked to nucleotides 1-11407. In principal it is possible to link any nucleotide sequence to nucleotides 1-11407 of SEQ ID NO:1, so claim 7 embraces all possible nucleotide sequences of at least about 15 nucleotides not present in SEQ ID NOS: 2 or 3. In fact, SEQ ID NO:1 was isolated from human chromosome 19, so claim 7 clearly embraces all isolated polynucleotides of at least about 15 nucleotides that can hybridize under stringent conditions to any sequence of human chromosome 19, that are not present in SEQ ID NOS: 2 or 3. The specification discloses SEQ ID NO:1 and its fragments. The specification fails to disclose a representative number of species of sequences of the claimed genus. For example, the specification fails to describe by structure, function, or correlation between structure and function, any chromosome 19 sequence other than SEQ ID NOS: 1-3 or their fragments, and as such fails to support claim 7 with an adequate written description. Note that SEQ ID NOS: 2 and 3 are outside of the claimed genus.

Enablement

Claims 1-6 are rejected under 35 U.S.C. 112, first paragraph. Claims 1-7 are not adequately enabled because the specification, while being enabling for isolated

polynucleotides having enhancer activity and comprising nucleotides 8021-8371 of SEQ ID NO:1, does not reasonably provide enablement for isolated polynucleotides comprising enhancers wherein the polynucleotides do not comprise nucleotides 8021-8371 of SEQ ID NO:1.

As discussed above, claims 1-5 are drawn to isolated polynucleotides with enhancer activity and containing 150 contiguous nucleic acids from nucleotides 1-11407 of SEQ ID NO:1 that are not present in SEQ ID NOS: 2 or 3. Claim 6 is drawn to isolated polynucleotides that have enhancer activity and comprise 150 contiguous nucleotides having at least about 70% identity to nucleotides 1-11407 of SEQ ID NO:1. Claim 7 is directed to isolated polynucleotides comprising at least about 15 nucleotides that hybridize under stringent conditions to a polynucleotide from nucleotides 1-11407 of SEQ ID NO:1. None of the sequences claimed in claims 1-6 can be a sequence present in SEQ ID NOS: 2 or 3. Because the specification teaches that the invention is intended to be a prostate-specific enhancer located within SEQ ID NO:1, or that is a sequence variant of SEQ ID NO:1, this rejection will focus on the sequences located in SEQ ID NO:1, and their variants, that can be used as enhancers.

The specification demonstrates that SEQ ID NO:1 contains an enhancer which is active in prostate cells expressing androgen receptors (LNCaP carcinoma cells), but is inactive in prostate-derived PC-3 carcinoma cells that lack androgen receptors, as well as in several other hormone responsive tissues including breast epithelia and carcinoma, and lung, liver, and colon carcinomas. Ectopic expression of androgen receptors in PC-3 cells was not sufficient to provide androgen-sensitive enhancer

activity in PC-3 cells, indicating that LNCaP cells have some other characteristic that is required for activity of the SEQ ID NO:1 enhancer. See paragraph 367. The specification provides no guidance as to the nature of this other characteristic.

Deletion analysis of SEQ ID NO:1 defines a core enhancer of 1172 bases from position 7200-8371 that has full enhancer activity (about 90-fold induction in LNCaP cells when linked to a minimal promoter). A minimal fragment from position 8021-8371 has reduced activity, (37-fold induction). This fragment contains an androgen response element (ARE) at bases 8192-8206 that is necessary but not sufficient for enhancer activity. A smaller fragment from position 8128-8263, which contains the same ARE, did not show any enhancer activity in LNCaP cells. See pages 101 and 102, and Figs. 24A and 24B. The specification states at page 106, lines 2-10 teaches that factors other than the ARE are required for function of the claimed enhancer, but provides no guidance as to what the nature of these factors.

A simple explanation of the data presented in the specification is that bases 8021-8127, and/or bases 8264-8371, comprise sequences that are required for enhancer function. Neither the specification nor the prior art provides specific guidance as to whether there are specific subsequences in these fragments that are required for enhancer function, nor guidance as to what alterations one can make in bases 8021-8127, and/or bases 8264-8371 while preserving enhancer function. In other words, no guidance is available as to particular transcription or accessory factors required for enhancer function, or to what sequences these factors may bind. Absent such guidance, one of skill in the art is left to trial and error experimentation in order to

determine what sequence fragments and variants of SEQ ID NO:1 will function as enhancers. One might argue that it would not be undue experimentation to construct and assay individual putative enhancers in order to determine empirically what sequence alterations are allowable. However as set forth in *In Re Fisher*, 166 USPQ 18(CCPA 1970), compliance with 35 USC 112, first paragraph requires:

> that the scope of the claims must bear a reasonable correlation to the scope of enablement provided by the specification to persons of ordinary skill in the art; in cases involving predictable factors, such as mechanical or electrical elements, a single embodiment provides broad enablement in the sense that, once imagined, other embodiments can be made without difficulty and their performance characteristics predicted by resort to **known scientific laws**; in cases involving unpredictable factors, such as most chemical reactions and physiological activity, scope of enablement varies inversely with the degree of unpredictability of the factors involved.

Emphasis added.

In this case there are no known scientific laws governing the sequences which are generally useful as enhancers, and the prior art and specification combined do not provide the requisite guidance that would allow one of skill in the art to make enhancers, other than those containing at least bases 8021-8371 of SEQ ID NO:1, without undue experimentation , i.e. either first discovering what factors are required for activity of the enhancer, where the binding sites for these factors are, and what sequence alterations in these sites are permitted, or alternatively screening random variants of SEQ ID NO:1 in order to find active enhancers.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claim 7 is rejected under 35 U.S.C. 102(b) as being anticipated by Schedlich et al (DNA 6(5): 429-437, (1987)).

Schedlich teaches an isolated polynucleotide comprising a sequence that is identical to bases 9786-11407 of SEQ ID NO:1. See attached alignment.

Thus Schedlich anticipates the claims.

Claim 14 is rejected under 35 U.S.C. 102(e) as being anticipated by US Patent 6,197,293.

US Patent 6,197,293, which was owned by Applicant at the time of the instant invention, claims adenoviral vectors comprising adenoviral genes required for replication, wherein the genes are under control of TREs. The specification teaches that the TRE may be an hKLK2-TRE. See paragraph 16.

Thus '293 anticipates the claims.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner(s) should be directed to Richard Schnizer, whose telephone number is 571-272-0762. The examiner can normally be reached Monday through Friday between the hours of 6:20 AM and 3:50 PM. The examiner is off on alternate Fridays, but is sometimes in the office anyway.

If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, Andrew Wang, can be reached at 703-306-3217 before 2/22/04, and at 571-272-0811 after 2/22/04. The official central fax number is 703-872-9306 until further notice. Inquiries of a general nature or relating to the status of the application should be directed to the Patent Analyst Trina Turner whose telephone number is 571-272-0564.

DAVE T. NGUYEN
PRIMARY EXAMINER

Richard Schnizer, Ph.D.